Acta Obstet Gynecol Scand 2003: 82: 850–856
Printed in Denmark. All rights reserved

Acta Obstetricia et Gynecologica Scandinavica
ISSN 0001-6349

ORIGINAL ARTICLE

Obstetric and neonatal risk of pregnancies after assisted reproductive technology: a matched control study

ZOLTÁN KOZINSZKY[1], JÁNOS ZÁDORI[2], HAJNALKA ORVOS[1], MÁRTA KATONA[3], ATTILA PÁL[1] AND LÁSZLÓ KOVÁCS[1]

From the [1]Department of Obstetrics and Gynecology, the [2]Center for Assisted Reproduction, Kaáli Institute, and the [3]Department of Pediatrics, University of Szeged, Albert Szent-Györgyi Medical and Pharmacological Center, Szeged, Hungary

Acta Obstet Gynecol Scand 2003; 82: 850–856. © Acta Obstet Gynecol Scand 82 2003

Background. The aim of the study was to evaluate the obstetric and neonatal outcome of pregnancies after assisted reproduction technology (ART) in comparison with matched controls from spontaneous pregnancies.
Methods. A total of 12 920 deliveries at the Department of Obstetrics and Gynecology, University of Szeged, from 1 January 1995 to 31 December 2001 were subjected to retrospective analysis. Two hundred and eighty-four singleton, 75 twin and 17 triplet pregnancies after ovulation induction ($n = 114$; 30.3%), intrauterine insemination ($n = 33$; 8.8%) and *in vitro* fertilization ($n = 229$; 60.9%) were evaluated. The pregnancy outcome of the singleton and twin pregnancies was compared with that for controls matched with regard to age, gravidity and parity and previous obstetric outcome after spontaneous pregnancies.
Results. Twenty-four percent of the assisted reproductive pregnancies were multiple pregnancies. The incidences of singleton intrauterine growth retardation (IUGR) and preterm birth were reasonably similar to those among the controls (IUGR: 6.3% vs. 4.2%; preterm births: 13.0% vs. 9.9%, for the cases and the controls, respectively). As compared with the controls, there was an increased incidence of cesarean section among the singleton (41.2% vs. 34.5%, $p = 0.12$; OR 1.33; 95% CI 0.95–1.87) and twin assisted reproduction pregnancies (66.7% vs. 60.0%), but without significant differences.
Conclusions. Increased obstetric risk could be observed concerning threatened preterm delivery and cesarean section rate in the study group. The perinatal outcome of singleton and twin pregnancies following assisted reproductive techniques is comparable with that of spontaneously conceived, matched pregnancies.

Key words: assisted reproduction; perinatal outcome; matched control study

Submitted 13 January, 2003
Accepted 04 March, 2003

The incidence of infertility is increasing worldwide (1) and a large range of assisted reproductive technology (ART) methods is available for the treatment of impaired fertility (2).

Reports on ART pregnancy outcome indicate that the frequencies of operative delivery, preterm birth, low birthweight and perinatal death are all greater than the general population-based incidences (3,4).

Many previous publications have stressed the higher incidences of prematurity, low birthweight, intrauterine growth retardation (IUGR), cesarean section, congenital anomalies, placenta previa and pregnancy-induced hypertension after *in vitro* fertilization–embryo transfer (IVF-ET)

Abbreviations:
ART: assisted reproductive technology; IUGR: intrauterine growth retardation; IVF-ET: in vitro fertilization–embryo transfer; NICU: neonatal intensive care unit; *SPSS*: Statistical Package for Social Sciences; OR: odds ratio; CI: confidence interval.

(5–11). Matched controls have also yielded adverse results with regard to IVF-ET (8,12–15) and ART (16,17).

The present retrospective study was designed to compare the perinatal data in singleton and twin pregnancies resulting from ART with matched naturally conceived pregnancies and to determine the obstetric risk in triplet pregnancies following ART.

Materials and methods

A retrospective analysis of 12 920 pregnancies that occurred between 1 January 1995 and 31 December 2001 was performed. The study group consisted of 376 (2.9% of the total) live pregnancies (284 singleton + 75 twin + 17 triplet pregnancies) resulting from various ART procedures at the Department of Obstetrics and Gynecology, University of Szeged. The rate of multiple births (24.5%) is higher among ART pregnancies than among naturally conceived pregnancies (1.45%) in our department. Details of the pregnancies and deliveries were obtained from medical records. The distribution of the antecedents of the singleton pregnancies was IVF-ET 180, ovulation induction 77 and intrauterine insemination 27; and that of the twin pregnancies IVF-ET 37, ovulation induction 32 and intrauterine insemination 6. The matched control group in which conception was spontaneous was selected on the basis of similarities in parity, gravidity, maternal age and previous obstetric outcome with regard to singletons and twins. The ratio between the patients and the controls was 1 : 1.

Potential controls were selected by systematically scanning the obstetric register for women of suitable age, parity and date of delivery. The control subjects were the next parturients on the list fullfilling the matching criteria. The relevant medical records were then retrieved and checked for the other matching criteria. When several patients could serve as potential controls, the patient best matching with regard to maternal height and weight was chosen. The matching criteria of the ART and control women were entered into a form and all forms were reviewed by one investigator for approval. To avoid any selection bias, the results of potential control pregnancies remained unread before the choice was made.

The triplet pregnancies (IVF-ET 12; ovulation induction 5) were analyzed without spontaneous controls filling the distribution of selected perinatal characteristics.

Deliveries were defined as all liveborn or stillborn babies delivered after 24 completed weeks of gestation. The gestational age at birth was calculated by adding 14 days to the day of ovum pick-up for the IVF-ET group, and by adding 14 days to the presumed day of ovulation for the ovulation induction group. For the spontaneous conception group, the first day of the last menstrual period was used. IUGR was defined as a birthweight below the 10th percentile for the gestational age, according to the sex and to the Hungarian data (18).

Congenital malformations were diagnosed by the same experienced neonatologist on the basis of physical examination, chest, abdominal or skull X-ray, and ultrasonography (cardiac, abdominal, head, etc.) according to the Hungarian registration of congenital anomalies (19). Birth defects were classified as major congenital malformations (e.g. congenital heart defects, gastrointestinal malformations, genitourinary tract malformations, bone malformations, etc.) or as minor anomalies (e.g. hypertelorism, low-set ears, polydactylia, etc.). Babies with major congenital or structural malformations were admitted to the neonatal intensive care unit (NICU) for further observation and treatment.

The following antepartum complications were examined: gestational diabetes mellitus, preeclamptic toxemia, pregnancy-induced hypertension, myoma, placenta previa, malpresentation, malposition, threatened premature labor, placental abruption, premature rupture of the membranes, intrauterine infection, meconium-stained amniotic fluid, oligohydramnios and polyhydramnios. The following intrapartum characteristics were assessed: cesarean section, fetal distress, cephalopelvic disproportion, retained placenta, prolonged labor and prolonged second stage.

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) 8.0 Windows program (SPSS Inc., Chicago, IL, USA). Univariate comparisons between singleton pregnancies were assessed by the paired *t*-test and the χ^2-test for continuous and categorical variables, respectively. Odds ratios (ORs) and 95% confidence intervals (CIs) were also calculated for categorical variables. Comparisons between twin groups were performed by the Mann–Whitney *U*-test and the Wilcoxon test for categorical and ordinal variables. The significance level was set at 5%, two-tailed.

Prematurity was defined as delivery before 37 weeks of gestation. Intrauterine infection was considered to exist when the mother had fever and leukocytosis and the fetus had tachycardia and postnatal symptoms of neonatal infection, e.g. tachypnoe, tachycardia, an oxygen demand and positive culturing. Fetal distress was defined

as the presence of repetitive late decelerations, severe variable decelerations and persistent fetal tachycardia. Placenta previa was defined as a placenta covering the internal os of the cervix and requiring delivery by cesarean section.

Results

Table I presents the pattern of pregnancy complications among the singleton groups. The two groups were comparable according to the proportions of primiparity and previous abortion. No statistical difference was found in the occurrence of gestational diabetes mellitus, intrauterine infection, inertia uteri, meconium-stained amniotic fluid, malpresentation or oligohydramnios. Threatened preterm delivery was significantly more common among the ART pregnancies (24.6% vs. 15.5%).

Table II shows the pregnancy characteristics among the twins. The differences in pregnancy characteristics between the cases and the controls were not significant statistically.

Table III gives an overview of the intrapartum complications in the two singleton groups. Premature rupture of the membranes, cephalopelvic disproportion and a prolonged second stage preceded labor more often in the spontaneous pregnancies, whereas cesarean section and retained placenta were more prevalent among the ART pregnancies, but without any significant differences.

Table IV details the intrapartum complications in the twin groups. The incidence of cesarean section was higher among the ART pregnancies, while premature rupture of the membranes and retained placenta were more common among the controls. Cephalopelvic disproportion, prolonged labor and prolonged second stage exhibited the same frequencies in the two groups.

Data on the neonatal outcome for the singleton pregnancies and the matched controls are listed in Table V. Although the gestational age and birthweight were lower, while the rates of preterm birth and IUGR were higher among the induced group, the differences did not reach the level of statistical significance. There were also slight but not significant increases in the occurrences of a worse 5-min Apgar score and congenital malformations. An unfavorable cord arterial blood pH <7.20 was more common among the controls.

The data on the neonatal outcome in the twin pregnancies are detailed in Table VI. A significant difference in birthweight ($p < 0.001$) was noted between the ART mothers and the matched controls who conceived naturally. There was no statistical difference in the pattern of gestational age, preterm birth and IUGR. There were slightly increased risks of an adverse 5-min Apgar score <7 and NICU admission, but without significant differences. The neonatal condition at birth, expressed either as the proportion of babies with an umbilical cord arterial pH < 7.20 or as an Apgar score <7 at 5 min after birth, was not significantly different in the two groups.

Table VII relates to the characteristics concerning the triplet pregnancies. Triplet pregnancies present a higher risk than that of either singleton or twin pregnancies with regards to the neonatal outcome. The rates of preterm birth, IUGR, low Apgar score, unfavorable cord arterial blood gas values and congenital malformations were extremely high. The proportions of cesarean section and

Table I. Pregnancy characteristics in singleton pregnancies

	ART group ($n = 284$) (32.3 ± 4.0 years)		Spontaneous group ($n = 284$) (32.0 ± 4.1 years)			
	n	%	*n*	%	*p*-value	OR (95% CI)
Primiparity	234	82.4	235	82.7	NS	0.98 (0.63–1.51)
Primigravidity	184	64.8	172	60.6	NS	1.20 (0.85–1.68)
Gestational diabetes mellitus	19	6.7	11	3.9	NS	1.79 (0.83–3.81)
EPH-gestosis	45	15.8	32	11.3	NS	1.48 (0.91–2.41)
Myoma*	2	0.7	5	1.8		
Placenta previa*	2	0.7	0	0.0		
Pregnancy-induced hypertension*	0	0.0	0	0.0		
Threatened preterm delivery	70	24.6	44	15.5	<0.05	1.78 (1.17–2.72)
Intrauterine infection	18	6.3	30	10.6	NS	0.57 (0.31–1.05)
Inertia uteri	218	76.8	197	69.4	NS	1.46 (1.00–2.12)
Meconium-stained amniotic fluid	42	14.8	43	15.1	NS	0.97 (0.61–1.54)
Malpresentation	20	7.0	16	4.6	NS	1.58 (0.77–3.24)
Oligohydramnios	9	3.2	20	7.0	NS	0.43 (0.19–0.97)
Polyhydramnios*	2	0.7	2	0.7		

*Statistical analysis was not meaningful
NS, not significant; OR, odds ratio; CI, confidence interval

Table II. Pregnancy characteristics in twin pregnancies

	ART group ($n=75$) (34.3 ± 3.9 years)		Spontaneous group ($n=75$) (33.9 ± 4.0 years)		
	n	%	*n*	%	*p*-value
Primiparity	29	38.7	38	50.7	NS
Primigravidity	42	56.0	47	62.5	NS
Gestational diabetes mellitus	7	9.3	9	12.0	NS
EPH-gestosis	16	21.3	14	18.7	NS
Myoma*	0	0.0	1	1.3	
Placenta previa*	0	0.0	1	1.3	
Pregnancy-induced hypertension*	0	0.0	1	1.3	
Threatened preterm delivery	53	70.7	56	74.7	NS
Intrauterine infection	4	5.3	6	8.0	NS
Inertia uteri	65	86.7	67	89.3	NS
Meconium-stained amniotic fluid	4	5.3	4	5.3	NS
Malpresentation	22	29.3	21	28.0	NS
Oligohydramnios*	1	1.3	1	1.3	
Polyhydramnios*	1	1.3	0	0.0	

*Statistical analysis was not meaningful
NS, not significant; OR, odds ratio; CI, confidence interval

threatened preterm delivery were also high compared with the singleton or twin pregnancies. The frequencies of edema proteinuria hypertension (EPH)-gestosis and premature rupture of the membranes did not differ significantly from those among the singleton or twin pregnancies.

Discussion

All of our data, relating to both the cases and the controls, were collected from the Department of Obstetrics and Gynecology. This helped to ensure that the data were as complete as possible and allowed the selection of a control group that was broadly similar and matched by age, previous parity, gravidity, multiplicity of pregnancies and previous abortions or pregnancies. The mothers were similar in ethnic origin and demographic background. A further advantage is that, as only one obstetric department was involved, the pregnancy management was similar throughout.

In any comparison of the perinatal outcome of ART pregnancies with that of pregnancies among the normal population, four factors must be borne in mind. Women who achieve pregnancy after ART are usually older than average; the proportion of elderly primigravid patients over the age of 35 years is fairly high. It is generally accepted that older women are more prone to obstetric problems (20–22), although some studies confirm this only in part (23). Further pregnancies among older women after ART do not have a worse outcome than that for spontaneously conceived pregnancies among women of the same age (24).

Most of the ART patients displayed primary infertility or even a previous adverse pregnancy outcome, including stillbirth, spontaneous abortion and extrauterine gravidity. In some studies, infertility has been shown to increase the risks of low birthweight, IUGR and preterm birth (4,25), but others (26–28) did not find such relationships.

Table III. Intrapartum characteristics in singleton pregnancies

	ART group ($n=284$)		Spontaneous group ($n=284$)			
	n	%	*n*	%	*p*-value	OR (95% CI)
Premature rupture of the membranes	92	32.4	114	40.1	NS	0.71 (0.51–1.01)
Cephalopelvic disproportion	16	5.6	21	7.4	NS	0.75 (0.38–1.46)
Retained placenta	24	8.5	16	5.6	NS	1.55 (0.80–2.98)
Prolonged labor	38	13.4	43	15.1	NS	0.87 (0.54–1.39)
Prolonged second stage	18	6.3	24	8.5	NS	0.73 (0.39–1.38)
Cesarean section	117	41.2	98	34.5	NS	1.33 (0.95–1.87)

NS, not significant; OR, odds ratio; CI, confidence interval

Table IV. Intrapartum complications in twin pregnancies

	ART group ($n=75$)		Spontaneous group ($n=75$)		
	n	%	*n*	%	*p*-value
Premature rupture of the membranes	31	41.3	41	54.7	NS
Cephalopelvic disproportion*	3	4.0	3	4.0	
Retained placenta	8	10.7	10	13.3	NS
Prolonged labor	6	8.0	9	12.0	NS
Prolonged second stage*	3	4.0	5	6.7	
Cesarean section	50	66.7	45	60.0	NS

*Statistical analysis was not meaningful
NS, not significant

Table V. Neonatal outcome in singleton pregnancies ART group

	ART group ($n=284$)		Spontaneous group ($n=284$)			
	n	%	*n*	%	*p*-value	OR (95% CI)
Gestational age (mean ± SD) (weeks)	38.31 ± 2.09		38.56 ± 2.10		NS	
Birthweight (mean ± SD) (g)	3175.8 ± 588.5		3268.4 ± 592.0		NS	
Preterm birth	37	13.0	28	9.9	NS	1.37 (0.81–2.30)
Intrauterine growth retardation	18	6.3	12	4.2	NS	1.53 (0.73–3.25)
Macrosomia (>4000 g)	16	5.6	29	10.2	NS	0.53 (0.28–0.99)
5-min Apgar score <7	9	3.2	5	1.8	NS	1.83 (0.60–5.52)
Cord arterial blood pH <7.20*	51/263	19.4	54/269	20.1	NS	0.96 (0.63–1.47)
NICU admission	12	4.2	12	4.2	NS	1.00 (0.44–2.27)
Congenital malformations	9	3.2	5	1.8	NS	1.83 (0.60–5.52)
Perinatal mortality†	0	0.0	0	0.0		

*Examination was not performed in every case. †Statistical analysis was not meaningful
NS, not significant; OR, odds ratio; CI, confidence interval

Table VI. Neonatal outcome in twin pregnancies

	ART group ($n=150$)		Spontaneous group ($n=150$)		
	n	%	*n*	%	*p*-value
Gestational age (mean ± SD) (weeks)	35.48 ± 3.01		35.49 ± 3.01		NS
Birthweight (mean ± SD) (g)	2361.5 ± 637.0		2297.3 ± 683.1		<0.001
Preterm birth	88	58.7	84	55.3	NS
Intrauterine growth retardation	28	18.7	29	19.3	NS
Macrosomia (>4000 g)†	0	0.0	0	0.0	
5-min Apgar score <7	22	14.7	21	14.0	NS
Cord arterial blood pH <7.20*	21/141	14.9	23/138	16.7	NS
NICU admission	36	24.0	35	23.3	NS
Congenital malformations†	5	3.3	2	1.3	
Perinatal mortality†	0	0.0	2	1.3	

*Examination was not performed in every case. †Statistical analysis was not meaningful
NS, not significant; OR, odds ratio; CI, confidence interval

The major factor contributing to an adverse pregnancy or obstetric outcome of ART as compared with a population-based control is the increased incidence of multiple pregnancy (29). In our study, multiplicity occurred in 24.5% of the ART pregnancies and in 2.5% of the spontaneous pregnancies in the study period. Concerning the obstetric outcome, the occurrence of twin pregnancy certainly increases the obstetric risk. Triplet pregnancies after ART methods involve the highest rate of complications as regards the pregnancy outcome. Most of the complications among ART pregnancies were associated with the high number of multiple pregnancies, whereas the rate of complications among the singleton ART parturients was not worse than the clinical average.

Table VII. Selected perinatal characteristics in triplet pregnancies ($n = 17$)

	n (34.9 ± 4.1 years)	%
Cesarean section*	17	100
Threatened preterm delivery*	15	88.2
EPH-gestosis*	3	17.6
Premature rupture of the membranes*	4	7.8
Preterm birth†	50	98.0
IUGR†	22	43.1
5-min Apgar score <7†	11	21.6
Cord arterial blood pH <7.20†‡	9/48	18.8
Congenital anomalies†	4	7.8

*Related to the number of the mothers. †Related to the number of the newborns. ‡Examination was not performed in every case

The effect of the ART method on the number of live births can be accurately evaluated by comparison with a matched control group. A certain proportion of ART pregnancies end as spontaneous abortions, induced terminations of pregnancy or extrauterine pregnancies; these were not evaluated in this study. The significantly low rate of congenital abnormalities observed in our clinic (2.5%) compared with the Hungarian average (4–5%) (18) was probably due to our more effective screening methods, which could diminish the rate of pregnancies with complications. At the same time, our clinic is a third-level center that attracts the higher risk pregnancies; this could explain the higher rate of various complications as compared with the Hungarian data (cesarean section: 20.6% vs. 20.2%; preterm birth: 13.2% vs. 8%, respectively, at our Department of Obstetrics and Gynecology and in Hungary overall) (18). However, the adverse data are involved in both the ART pregnancies and the randomly and blindly selected matched controls.

It is clinically significant that ART pregnancies involve increased risks for both the mothers and the infants, as the rates of obstetric complications among singleton, twin and triplet ART pregnancies are higher than the clinical averages for spontaneous pregnancies. Overall, our results suggest that in the case of singleton and twin pregnancies the ART methods do not present an extra risk as concerns the obstetric outcome. The incidence of perinatal complications is slightly higher among ART pregnancies as compared with the matched controls, but the difference is not statistically significant.

Many reports involving matched controls have drawn attention to the high incidence of preterm deliveries and IUGR after ART (16,17) or IVF-ET (8,12,14), but this has not been demonstrated among IVF-ET pregnancies by other studies (13,15). In our study, the incidences of IUGR and premature delivery proved to be higher after ART, but without any statistical difference.

In the literature reports, more patients were delivered by cesarean section in the study group than in the controls (8,12–17). We did not observe a major difference in the rate of cesarean section between the ART pregnancies and the control parturients. The higher cesarean section rate in the study group (as compared with the clinical data) is explained mainly by the increase in elective cesareans because of the older age of the primiparous women and reflects the anxiety of the physicians.

In some previous matched control studies, the mean gestational age and mean birthweight at delivery were significantly lower in ART or IVF-ET infants (8,12,14,16) or neonates of twins (15). Other studies did not find the same result (13,17).

In contrast with earlier corresponding studies, we found no major differences in respect of gestational age, birthweight, rate of malformations or NICU admission, with the exception of the birthweight following twin pregnancies, where the babies in the ART group exhibited a higher birthweight.

The results of the present study do not confirm higher incidences of pregnancy-induced hypertensive disorders or placenta previa. Pregnancy-induced hypertension and placenta previa occurred in very low numbers among the ART pregnancies, in contrast to the conclusions of previous ART (16) and IVF-ET studies (8,12).

References

1. Testart J, Plachot M, Mandelbaum J, Salat-Baroux J, Frydman R, Cohen J. World collaborative report on IVF-ET and GIFT: 1989 results. Hum Reprod 1992; 7: 362–9.
2. Brinsden PR. A textbook of *in vitro* fertilization and assisted reproduction, 2nd ed. London: The Parthenon Publishing Group, 1999: 34.
3. Beral V, Doyle P. MRC working party on children conceived by *in vitro* fertilisation. Births in Great Britain resulting from assisted conception, 1978–87. Br Med J 1990; 300: 1229–33.
4. Ghazi HA, Spielberger C, Kallen B. Delivery outcome after infertility – a registry study. Fertil Steril 1991; 55: 790–4.
5. Lancaster PAL. Australian In Vitro Fertilization Collaborative Group. High incidence of preterm births and early losses in pregnancy after IVF. Br Med J 1985; 291: 1160–3.
6. Doyle P, Beral V, Maconochie N. Preterm delivery, low birth weight and small-for-gestational-age in liveborn singleton babies resulting from in-vitro fertilization. Hum Reprod 1992; 7: 425–8.
7. Seoud MA, Toner JP, Kruithoff C, Muasher SJ. Outcome of twin, triplet and quadruplet *in vitro* fertilization pregnancies: the Norfolk experience. Fertil Steril 1992; 57: 825–34.
8. Tan SL, Doyle P, Campbell S, Beral V, Risk B, Brinsden P. Obstetric outcome of in-vitro fertilization pregnancies

compared with normally conceived pregnancies. Am J Obstet Gynecol 1992; 167: 778–84.
9. Olivennes F, Rufat P, André B, Pourade A, Quiros MC, Frydman R. The increased risk of complications observed in singleton pregnancies resulting from in-vitro fertilization (IVF) does not seem to be related to the IVF method itself. Hum Reprod 1993; 8: 1297–300.
10. Rufat P, Olivennes F, de Mouzon J, Dehan M, Frydman R. Task force report on the outcome of pregnancies and children conceived by *in vitro* fertilization, France 1987–1989. Fertil Steril 1994; 61: 324–33.
11. Wang JX, Clark AM, Kirby CA, Philipson G, Petrucco O, Anderson G. The obstetric outcome of singleton pregnancies following *in vitro* fertilization/gamete intra-fallopian transfer. Hum Reprod 1994; 9: 141–6.
12. Verlaenen H, Cammu H, Derde MP, Amy JJ. Singleton pregnancy after in-vitro fertilization: expectations and outcome. Obstet Gynecol 1995; 86: 906–10.
13. Reubinoff BE, Samueloff A, Friedler S, Schenker JG, Lewin A. Is the obstetric outcome of *in vitro* fertilized singleton gestations different from natural ones? A controlled study. Fertil Steril 1997; 67: 1077–83.
14. Koudstaal J, Braat DDM, Bruinse HW, Naaktgeboren N, Vermeiden JPW, Visser GHA. Obstetric outcome of singleton pregnancies after IVF: a matched control study in four Dutch University hospitals. Hum Reprod 2000; 15: 1819–25.
15. Koudstaal J, Bruinse HW, Helmerhorst FM, Vermeiden JPW, Willemsen WNP, Visser GHA. Obstetric outcome of twin pregnancies after in-vitro fertilization: a matched control study in four Dutch University hospitals. Hum Reprod 2000; 15: 935–40.
16. Tanbo T, Dale PO, Lunde O, Moe N, Åbyholm T. Obstetric outcome in singleton pregnancies after assisted reproduction. Obstet Gynecol 1992; 86: 188–92.
17. Dhont M, De Sutter P, Ruyssinck G, Martens G, Bekaert A. Perinatal outcome of pregnancies after assisted reproduction: a case-control study. Am J Obstet Gynecol 1999; 181: 688–95.
18. Demographic Year Book. (In Hungarian.) Budapest: Hungarian Statistical Office, 2002: 145.
19. EUROCAT Central Registry. Report on methodological workshop. Brussels. 1995.
20. MacDonald IR, MacLennan H. A consideration of the treatment of elderly primigravidae. J Obstet Gynaecol Br Commonw 1960; 67: 443–50.
21. Booth RT, Williams GL. Elderly primigravidae. J Obstet Gynaecol Br Commonw 1964; 71: 249–54.
22. Kessler I, Lancet M, Borenstein R, Steinmetz A. The problem of the older primipara. Obstet Gynecol 1980; 56: 165–9.
23. Kozinszky Z, Orvos H, Zoboki T, Katona M, Wayda K, Pal A et al. Risk factors for cesarean section of primiparous women aged over 35 years. Acta Obstet Gynecol Scand 2002; 81: 313–16.
24. Kozinszky Z, Orvos H, Katona M, Zoboki T, Pal A, Kovacs L. Perinatal outcome of induced and spontaneous pregnancies of primiparous women aged 35 or over. Int J Gynaecol Obstet 2002; 76: 23–6.
25. Williams MA, Goldman MB, Mittendorf R, Monson RR. Subfertility and the risk of low birth weight. Fertil Steril 1991; 56: 668–71.
26. Tuck SM, Yudkin PL, Turnbull AC. Pregnancy outcome in elderly primigravidae with and without a history of infertility. Br J Obstet Gynaecol 1988; 5: 230–7.
27. Li TC, Macleod I, Singhal V, Duncan SL. The obstetrics and neonatal outcome of pregnancy in women with previous history of infertility. Br J Obstet Gynecol 1991; 98: 1087–92.
28. Bonduelle M, Liebaers I, Deketerlaere V, Derde M-P, Camus M, Devroey P et al. Neonatal data on a cohort of 2889 infants born after ICSI (1991–1999) and of 2995 infants born after IVF (1983–1999). Hum Reprod 2002; 3: 671–94.
29. Bergh T, Ericson A, Hillensjö T, Nygren K-G, Wennerholm U-B. Deliveries and children born after in-vitro fertilization in Sweden, 1982–95: a retrospective cohort study. Lancet 1999; 354: 1579–85.

Address for correspondence:
László Kovács
H-Szeged
Semmelweis u. 1
Hungary
e-mail: kovacs@obgyn.szote.u-szeged.hu